

We claim:

1. A method of diagnosing or predicting susceptibility to a clinical subtype of Crohn's disease characterized by fibrostenosing disease, comprising
5 determining the presence or absence in an individual of a fibrostenosis-predisposing allele linked to a NOD2/CARD15 locus,

10 wherein the presence of said fibrostenosis-predisposing allele is diagnostic of or predictive of susceptibility to the clinical subtype of Crohn's disease characterized by fibrostenosing disease.

2. The method of claim 1, wherein said
15 clinical subtype of Crohn's disease is characterized by fibrostenosing disease independent of small bowel involvement.

3. The method of claim 1, wherein said
20 fibrostenosis-predisposing allele is located within said NOD2/CARD15 locus.

4. The method of claim 3, wherein NF-kappa B activation by a NOD2/CARD15 polypeptide encoded by said
25 fibrostenosis-predisposing allele is reduced as compared to NF-kappa B activation by a wild-type NOD2/CARD15 polypeptide.

5. The method of claim 3, wherein said
30 fibrostenosis-predisposing allele is located in a coding region of said NOD2/CARD15 locus.

6. The method of claim 5, wherein said
35 fibrostenosis-predisposing allele is located in a region encoding residues 744 to 1020 of NOD2/CARD15.

7. The method of claim 5, wherein said fibrostenosis-predisposing allele is a "2" allele at a SNP selected from SNP 8, SNP 12, and SNP 13.

5 8. The method of claim 7, wherein said fibrostenosis-predisposing allele is a "2" allele at SNP 13.

10 9. The method of claim 3, wherein said fibrostenosis-predisposing allele is located in a non-coding region of said NOD2/CARD15 locus.

15 10. The method of claim 9, wherein said fibrostenosis-predisposing allele is selected from a JW1, JW15, and JW16 variant allele.

20 11. The method of claim 9, wherein said fibrostenosis-predisposing allele is located in a promoter region of said NOD2/CARD15 locus.

12. The method of claim 11, wherein said fibrostenosis-predisposing allele is an allele selected from a JW17 and JW18 variant allele.

25 13. The method of claim 1, comprising determining the presence or absence in said individual of at least two fibrostenosis-predisposing alleles linked to a NOD2/CARD15 locus,

30 wherein the presence of one or more of said fibrostenosis-predisposing alleles is diagnostic of or predictive of susceptibility to the clinical subtype of Crohn's disease characterized by fibrostenosing disease.

14. The method of claim 13, wherein said at least two fibrostenosis-predisposing alleles are "2" alleles at a SNP selected from SNP 8, SNP 12, and SNP 13.

5 15. The method of claim 14, comprising determining the presence or absence in said individual of

(i) a "2" allele at SNP 8,

10 (ii) a "2" allele at SNP 12, and

(iii) a "2" allele at SNP 13,

15 wherein the presence of one or more of said "2" alleles at SNP 8, SNP 12, and SNP 13 is diagnostic of or predictive of susceptibility to the clinical subtype of Crohn's disease characterized by fibrostenosing disease.

20 16. The method of claim 1, wherein said fibrostenosis-predisposing allele is associated with said clinical subtype of Crohn's disease characterized by fibrostenosing disease with an odds ratio of at least 2 and a lower 95% confidence limit greater than 1.

25 17. The method of claim 1, further comprising generating a report indicating the presence or absence in said individual of said fibrostenosis-predisposing allele.

30 18. The method of claim 1, further comprising generating a report indicating the presence or absence in said individual of said clinical subtype of Crohn's disease characterized by fibrostenosing disease.

19. The method of claim 1, wherein determining the presence or absence of said fibrostenosis-predisposing allele comprises enzymatic amplification of nucleic acid from said individual.

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20. The method of claim 19, wherein said amplification is polymerase chain reaction amplification.

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21. The method of claim 20, wherein said polymerase chain reaction amplification is performed using one or more fluorescently labeled probes.

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22. The method of claim 20, wherein said polymerase chain reaction amplification is performed using one or more probes comprising a DNA minor groove binder.

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23. A method of optimizing therapy in an individual, comprising

(a) determining the presence or absence in said individual of a fibrostenosis-predisposing allele linked to a NOD2/CARD15 locus,

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(b) diagnosing individuals in which said fibrostenosis-predisposing allele is present as having a fibrostenosing subtype of Crohn's disease, and

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(c) treating said individual having a fibrostenosing subtype of Crohn's disease based on said diagnosis.